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EDITORIAL

LET THE OUTLOOK BE BROAD

THOSE who would practise the healing arts, be their prospective patients men or animals, have to undergo a long period of training and follow a curriculum which demands more than a passing knowledge of many sciences and subjects. The course is founded upon the study of natural history, i.e., Biology, so that the student may comprehend the more specialised or vocational subjects which follow. It can be called a liberal training. The student is not expected to attain the status of an expert in any particular subject, but to acquire a reasonable knowledge of each and every aspect of his studies so that he can pass smoothly and with understanding through the various facets which lead to the final effort when he gains the right to practice the art and science of his profession.

The sphere of activity of a Veterinary Surgeon is much wider than that of his colleague who deals with men alone. Those who designed the course of study for veterinary surgeons were wise in their generation when they based the training on broad biological principles. Veterinary Science, Human Medicine and Agricultural Science all belong to the discipline of Biology. In consequence they have much in common, and a considerable degree of integration can be to their mutual advantage.

The connection between Veterinary Science and Agriculture and between Veterinary Science and Human Medicine has been recognised and accepted for a long time, but the connection between Human Medicine and Agriculture seems to have escaped general notice. Modern medical training has been criticised in that it has become too circumscribed and the product of the schools

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has little knowledge of the works of nature other than as they are manifested in a sick man. The tradition and clinical skill of Hunter, Osler, Bland-Sutton, Dawson and Hutchison, men with a superb knowledge of natural history, has been at a discount, swamped by the prestidigitations of the ubiqitous laboratory report. This is a matter for regret.

One would be foolish not to recognise the value of modern technical aids to diagnosis, but their value would be enhanced if supported by clinical skill based on a wide knowledge of plant and animal life. Veterinary Science is the link between the Agriculturalist, the Naturalist and Human Medicine, and one way of implementing that bridge is to foster and encourage the exchange of information and ideas between doctors and veterinary surgeons.

About thirty years ago Sir Frederick Hobday and Sir Clifford Allbutt, both enthusiastic supporters of this view, were able to persuade the Royal Society of Medicine to establish a section of Comparative Medicine in which medical men and veterinary surgeons could meet on an equal footing for free discussion and the exchange of ideas. The Section has fulfilled many of its sponsors' hopes, and it has been one of the most popular sections in the Society.

In one respect the original conceptions of the founders have not been fulfilled completely. It was hoped that clinicians would play a large part in this, but that has not been the case and the stage has been passed to the specialist worker and some of the discussions have been of value only to those who work in a limited field.

The fault lies with the clinicians and particularly those of the Veterinary profession. It is hoped that more will join the section and play a full part in the meetings and discussions. No profession can exist without its quota of those who practice both the art and science. Their knowledge and experience is great and is just as valuable as that which is conceived in a laboratory.

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GENERAL ARTICLES

FIELD TRIALS WITH B.C.G. FOR THE IMMUNISATION OF CALVES AGAINST TUBERCULOSIS*

An Account of Experiments Carried Out on Behalf of the Agricultural Research Council's Technical Committee on Tuberculosis in Animals

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A COMPREHENSIVE series of controlled laboratory experiments was made at the Institute of Animal Pathology, Cambridge, from 1926 to 1940 on the value of B.C.G. in protecting cattle against a heavy artificial infection with *Mycobacterium tuberculosis*.

The Agricultural Research Council had afforded considerable financial assistance, and after these experiments were made they were advised by the Joint Standing Committee on Tuberculosis, appointed by the Medical Research Council and the Agricultural Research Council, that sufficient evidence was available to warrant a large-scale field trial to determine the value of the vaccine when applied on farms where the herds were heavily infected with tuberculosis. The following report summarises the results obtained from two field experiments, one commenced in 1935 and ended in 1946, while the other began in 1942 and has just been completed.†

Studies of B.C.G. have fallen under two main headings: (*a*) the harmlessness of the vaccine, and (*b*) the immunising value of the vaccine. The Committee decided to review the available evidence before embarking on the costly and complex trials which would be required, and the first section of the report covers a brief summary of the main articles up to 1938. No attempt has been made to abstract the voluminous literature which has developed from 1923 to the present date.

Brief Summary of the Evidence of the Value of B.C.G. Vaccine

(*a*) *The innocuousness of the vaccine*

After a period of active controversy on the harmlessness of B.C.G. a stage has been reached at which most reputable workers are agreed that B.C.G. does

* The field trials were supervised by the late Dr. L. Jordan, M.R.C.V.S., Agricultural Research Council; R. Renfrew, M.R.C.V.S., Animal Health Division of the Ministry of Agriculture; J. C. Meikle, M.R.C.V.S., Agricultural Research Council; and E. Clark, M.R.C.V.S., D.V.S.M., Animal Health Division of the Ministry of Agriculture.

† The full report and tables can be obtained on request from the Agricultural Research Council, Cunard Building, 15 Regent Street, London, S.W.1.

not produce progressive tuberculosis. It may be mentioned in passing that it was not maintained even by the first workers that B.C.G. is incapable of producing lesions in the animal body, but it was claimed that such lesions are benign and unable to develop into active centres of tuberculosis. This contention was reiterated on many occasions by Calmette, but doubts were cast on the validity of this view by later authors (Petroff, Branch and Steenken, 1929; Watson, McIntosh and Konst, 1928; and others).

At the present time there is general agreement that, although some substrains of B.C.G. which may have been cultivated up to 1936 in a manner other than that recommended by Calmette contained virulent mutants, those which are now used for vaccine production are completely harmless (Irvine, 1949).

(*b*) *Immunising value of the vaccine*

An assessment of the efficacy and duration of the immunity produced by the vaccine is difficult. Many opposed points of view have been advanced; even now the problem cannot be regarded as solved.

There is an increasing recognition of the use of the vaccine as a valuable adjunct in measures designed to protect the young adult against fulminating primary tuberculosis, but the experience in the human subject may have little or no bearing on the control of tuberculosis in cattle.

The preliminary experiments of Calmette and Guérin (1920, 1924, 1928) indicated that after vaccination cattle possessed a solid immunity against a test dose of virulent organisms. Other investigations which were undertaken in different parts of the world are difficult to assess owing to the wide variations in dosage and routes of vaccination and in methods of challenge ranging from an intravenous injection of a virulent culture to the exposure to naturally-infected animals. The conditions were frequently so different that an exact comparison is impossible.

The various views which have been expressed may be considered under three headings. The first group comprises those workers who failed to find any increased resistance as a result of the injection of B.C.G. The experience of Watson is perhaps typical in this respect. As a result of his final experiments, Watson (1934) reached the conclusion that up to a period of five and a half years of age the incidence of tuberculosis in the aggregate was the same in vaccinated and unvaccinated cattle. The average degree of tuberculosis was less in young vaccinated animals but greater in the maturing animals in the vaccinated class. He stated that a decline in resistance was most likely to occur between puberty and maturity—in animals from two to four years old. A second group of workers adopts a middle course in admitting that some increased resistance is manifested by the use of the vaccine. According to these there is a marked difference between the extent of the lesions in vaccinated and control animals. In the latter the lesions are often acute and progressive, whereas in the former they are insignificant or chronic in nature. No claim is made that an absolute immunity develops. The third group considers that vaccination affords complete protection against natural infection, and that the influence of B.C.G. is so potent that it will effectively prevent the ingress and establishment within the body of virulent tubercle bacilli. Doubtless the variations in these results can be explained, in some measure, by differences in the methods of conducting these experiments, but this supposition will not afford a complete explanation of the wide discrepancies.

In the early trials of Calmette and Guérin, which were sometimes relatively short, a high degree of protection was afforded against an artificial infection; moreover, subsequent field experiments by a number of workers appeared to confirm the efficiency of the vaccine when applied on infected farms in France, Austria, Italy, the Ukraine, and elsewhere. The results appear to substantiate the claim made by Calmette that considerable progress in the eradication of tuberculosis

from infected herds was possible by a systematic application of the vaccine to all young stock.

The experimental work by Canadian and American workers from 1926 to 1936 was not conclusive. In Canada, Rankin (1928), Rankin, Ower, Shaw, Talbot and Vango (1932) undertook extensive trials on calves and reported that the lesions in vaccinated animals subsequently exposed to infection were much less extensive than in the controls. Watson (1930, 1933, 1934), however, formed the opinion that age incidence plays an important part. He asserts that whereas cattle killed one and a half years after exposure to infection showed complete or nearly complete protection (92.3 per cent in vaccinated and 74.1 per cent in the controls), the incidence in the two groups after an average period of exposure of four and a half years was 42.1 per cent and 56.2 per cent respectively, a figure which favoured the controls. Similar discrepant results have been reported from the U.S.A.

In England controlled experiments on the value of B.C.G. were made at the Institute of Animal Pathology, Cambridge. These comprised studies on the best routes for administering the vaccine (Buxton and Griffith, 1931), trials on the duration of immunity induced by two doses given intravenously (Griffith, Buxton and Glover, 1931), and on the effect of revaccination at intervals of six, nine and twelve months after primary vaccination (Buxton, Glover and Griffith, 1934).

Finally, a relatively large-scale experiment was made to test the effect of repeated doses of B.C.G. at intervals with immediate or delayed exposure to infection; the conditions simulated, as far as possible, those encountered on infected farms (Buxton, Glover, Dalling and Bosworth, 1939).

The results showed that B.C.G. given intravenously at six-monthly intervals in doses of 50 or 100 mg. was well tolerated by cattle. When protected from exposure to gross infection most of the animals were completely resistant to a test dose which produced extensive local and slight generalised tuberculosis in unprotected controls. The resistance induced by the repeated inoculation of B.C.G. over a period of three years was, however, overcome by continued exposure to infection immediately after the first dose of vaccine or after a lapse of 18 months.

Field Trials in Great Britain

The field trials of B.C.G. have been made in two stages. The two experiments are described separately under the headings " West Sussex Investigation " and " Berkshire Investigation."

West Sussex Investigation

The project was approved by the Joint Committee on Tuberculosis, and the necessary funds were made available by the Agricultural Research Council. In 1935 a group of tuberculin-tested calves from Ayrshire was vaccinated intravenously with B.C.G. at the Institute of Animal Pathology, Cambridge, and was then split into groups which were distributed in herds heavily infected with tuberculosis.

History of farms and the arrangements

Farm T. comprised about 80 milking cows. A tuberculin test in 1937 showed that 70 per cent were positive reactors, and in 1939 all were positive. Tuberculosis continued to take a heavy toll of the herd, and in 1937, 1938 and 1939 the number of animals seized under the Tuberculosis Order was 3, 6 and 3 respectively. Two experimental animals only remained in 1940 and the owner sold the residue of his reactor animals in December, 1940.

Farm B. was a mixed commercial herd of about 40 cows. Bovine tuberculosis was known to have existed in the herd both before and during the experiment. During 1937-1939 the number of animals taken under the Tuberculosis Order from this herd was 0, 3 and 0 respectively. Several changes in staff made it difficult to follow up the contact stock and the owner also weeded out his cattle ruthlessly.

Farm P. This was a commercial herd from which many wasters were sent to the knackers every year. Unlike farms B. and T., the premises were dark, of poor construction, overcrowded and very badly ventilated. The experimental animals received the same treatment as the home-bred stock, using the same fields, hovels and feeding utensils and finally calved down under identical conditions. During 1937-39 the number of animals taken under the Tuberculosis Order from this herd was 0, 2 and 0 respectively. There was no material change in conditions on this farm during the trials.

Farm L. Two separate sets of premises were used for this herd. On one farm, buildings were extremely bad and infection could spread easily. The vaccinated animals received similar treatment to the rest of the herd and had every opportunity to pick up the infection. Before the experiment many animals were taken from this herd under the Tuberculosis Order, and during 1937-1939 the numbers were 1, 0 and 2 respectively. Since 1940 the owner had attempted the eradication of tuberculosis by segregation of young stock, repeated testing of young animals and eradication of reactors. In 1946 the complete eradication of tuberculosis was achieved by disposal of the reacting cows.

On the other farm the premises were much better but the cows were not allowed out of doors in the winter. In 1935 seven animals from this farm were slaughtered under the Tuberculosis Order. The experimental animals were well mixed throughout the herd and received normal treatment. During 1937-1939 the number of animals taken from this herd under the Tuberculosis Order was 0, 4 and 3 respectively.

Vaccination

During the whole of the period the experimental animals received reinforcing doses of B.C.G. (50 mg. in 10 c.c.) intravenously at intervals of approximately six months. The intervals were kept as regular as possible but twice in 1940 and in 1942 they extended to almost ten months.

The injections were usually carried out without trouble and with no untoward results, but on one occasion there was a marked reaction in a small group. Within fifteen minutes of injection the animals showed considerable respiratory distress, the head was held with nose poked forward, legs splayed, nostrils dilated and breathing was very fast and laboured. These symptoms subsided after about thirty minutes and the animals gradually became normal. One owner complained that the milk yield dropped considerably after the inoculation and that it remained low afterwards, unless the cows could be grazed on a good fresh pasture immediately. No complaints were received from other owners.

Controls

Farm T.—No form of control was possible on this farm because of the attempt being made to form a T.T. unit with the appropriate isolation of home-bred young stock. The experimental animals were housed in premises containing over 60 animals, all of which were known to be positive reactors.

Farm B.—Up to 1940 there were 19 animals in the same age group as the experimental ones and they had spent their lives in more or less constant contact. Two of them were destroyed under the Tuberculosis Order and four others were fattened and sold. Because of changes in the stock it was not possible to keep records, but three cows were removed under the Tuberculosis Order.

Farm P.—During 1936-37 the experimental animals had contact at some time or other with 49 other animals of approximately the same age; of these 13 were discarded. Later they had similar contact with 24 home-bred animals of which four were eliminated in 1938 and two in 1939. Eventually of 38 controls, 25 were sold fat, five were affected with Johne's disease, three were destroyed owing to tuberculosis and one died. Four were not traced.

Farm L.—There were 60 controls on this farm: four were condemned on account of advanced tuberculosis, and nine were removed for other reasons. Eventually 36 were sold fat, nine were severely affected with tuberculosis, five were suffering from Johne's disease. Several more were removed for other reasons.

Post-mortem examinations

In the initial stages of the field trial, the owners in whose herds the vaccinated animals were placed, were keenly interested in the response of the vaccinated group to exposure to infection. If an animal was eliminated either by sale or by slaughter, the change was notified and an opportunity was thus afforded of keeping track of the vaccinated animals. During the later stages, however, and particularly during the war period, an increasing number was lost to the experiment through a variety of causes.

In some instances the post-mortem evidence was obtained indirectly from a meat inspector. In most other cases the organs and glands were carefully examined for macroscopic evidence of tuberculosis. Representative samples including glands of the head, thorax, and abdomen, and superficial carcass glands together with portions of any suspicious organs were forwarded to the laboratory for biological examination. Portions of glands were ground with saline solution and inoculated into guinea-pigs. The number for each set of organs and glands varied from 6 to 14. Guinea-pigs which did not die were killed between the fourth and six month after injection. Of the 47 animals distributed at the commencement of the trial, 12 were examined post-mortem but no material was available for further tests, 21 were examined biologically, and 14 were disposed of and post-mortem examinations were not made. In the

TABLE 1

Extent of Tuberculosis in Vaccinated Animals

Farm	Total vaccinated	No biological test		Biological test		Lost to experiment
		Positive +	Negative −	Positive +	Negative −	
T.	8		1		5	2
B.	10			2	3	5
P.	10	3	2	1	4	
L.	19	2	4	1	5	7
	47	5	7	4	17	14

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group of 33 which were examined, nine showed lesions of tuberculosis and 24 were negative. Two of the tuberculous animals (376 and 379) were extensively affected, while in the remaining six the lesions were moderate to trivial. The results are in Table 1.

The results obtained on all the farms show that, of 33 vaccinated animals which were autopsied, nine showed lesions of tuberculosis. Of 116 contact controls, 19 were seized under the Tuberculosis Order and 61 were known to be affected with tuberculosis. Tuberculin tests showed the incidence to be nearly 100 per cent.

Berkshire Investigation

In 1942, at a time when the Ministry of Agriculture felt that owing to war conditions it was not possible to proceed with the scheme for encouraging owners to eliminate tuberculosis and thus to become attested at the rate which was envisaged in 1938 and 1939, the National Farmers Union made enquiries whether the eradication of the disease could be hastened by the use of B.C.G. It was represented that many farmers had followed with interest the investigations in West Sussex and abroad, and that if the Agricultural Research Council would recommend the vaccine, no difficulty would be experienced in finding owners willing to vaccinate their herds.

The Tuberculosis Committee considered the matter and felt that the information available about the use of the vaccine under ordinary farming conditions was totally inadequate to permit it to recommend B.C.G. for general use. A case had been made, however, for extended field trials by a worker in the full-time employment of the Council. It thought that information of value could be obtained only from experiments of long duration undertaken in herds where there was evidence of a high initial incidence of clinical tuberculosis.

Various schemes were considered. The trials which were likely to give evidence which could be examined statistically were those in which a proportion of vaccinated and unvaccinated animals were exposed to infection in heavily-infected herds. Such trials, however, could only be undertaken at considerable expense, and the number of herds available was likely to be very limited. In view of the urgency of endeavouring to control bovine tuberculosis, it was felt that a less ambitious programme should be applied on a much more extensive scale in which, as will be explained, it would be possible to obtain uncontrolled evidence of the efficacy of B.C.G. and at the same time to secure a significant reduction in the amount of the disease.

The object of the scheme was to apply B.C.G. vaccine to heavily-infected herds in which eradication of the disease by other methods was considered impracticable. It was thought that many owners who were anxious to take advantage of the Ministry of Agriculture's Attested Herds Scheme were unable to take this step on account of an initial heavy infection or for other reasons, and would welcome an alternative scheme of reducing infection. It was hoped to ascertain whether B.C.G. could be applied under conditions obtaining in this country and would effect a significant reduction in tuberculous infection within

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a reasonable period of time, a reduction which would itself be of practical value or would be sufficient to enable an owner to take advantage of the Attested Herds Scheme. In making a choice of herds attention was paid not only to the weight of infection as revealed by tuberculin tests, but also to the clinical history of the herds. As far as possible the vaccinated herds were selected by random sampling, although some degree of selection was practised in order to secure the co-operation of farmers who were the most likely to accept all measures suggested under the Scheme.

In the herds chosen for vaccination, a preliminary tuberculin test was applied to ascertain the extent of infection, after which the calves were separated from their mothers and tuberculin tested at about three months of age. Those calves which gave a positive reaction were removed from the herd, whilst every calf which failed to react was vaccinated and revaccinated at six-monthly intervals. On reaching maturity these were drafted into the main herd which was thus gradually changed into one completely composed of vaccinated animals. It was hoped that vaccination would cease as soon as every unvaccinated animal in the original herd had been eliminated, after which calves born on the farm or tubercle-free stock introduced from outside would be admitted without vaccination.

The scheme was primarily concerned with the creation of groups of cattle which had been rendered resistant to tuberculosis at an early age.

Some of the farmers who participated wished, however, to expedite the eradication of active infection and they were permitted to introduce heifers negative to the tuberculin test which were vaccinated before admission to the immunised herd and revaccinated at intervals of six months.

As success would depend to a large extent on a close and constant supervision of the herds, which, as far as possible, should be self-contained, it was essential that any area selected should be suitable dairying country so as to facilitate administration.

At first the counties of Berkshire and Oxford were selected for the trial and most of the farms eventually brought into the scheme were in these areas; later a few farms in other parts of the country were included.

Whilst self-contained herds known to be heavily infected with tuberculosis were those primarily considered, others where the incidence was not known were included, as it was considered that the type of owner necessary for efficient co-operation was as important as the suitability of his herd. Moreover, it was considered desirable to include not only herds of various sizes, breeds and quality, but also herds with different degrees of infection.

Vaccination

The vaccine was given by the intravenous route only to calves which were non-reactors to tuberculin. It was intended to vaccinate at once all the calves if the preliminary test revealed no tuberculin-positive animals, and, in cases where the reactors in a group did not exceed 25 per cent, to isolate and retest the non-reactors in approximately two months. This procedure, however, reduced the number of animals it was possible to vaccinate immediately after

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the preliminary test. In many instances, because of the presence of a very small number of reactors, non-reacting animals had to remain unvaccinated, and were subjected to the risk of infection whilst awaiting retest. The rigid rules previously agreed to were therefore relaxed. This allowed greatly increased numbers of animals to be vaccinated immediately the results of the tuberculin test were known, and was obviously of the greatest encouragement to the owners concerned. The danger of vaccinating an animal in the pre-allergic stage, with possibly undesirable consequences, was realised, but since this risk was always present in an infected herd, it was considered that the more flexible method was justified.

Results

The first calves were vaccinated in 1942, and the trials ended in 1952. By then herds which originally entered the scheme or were accepted at an early stage had either been attested or had received a T.T. licence, or had withdrawn for reasons which will be given later.

A few herds had been accepted at a later stage when the tuberculosis situation in herds in general had undergone a significant change owing to the increased interest shown by farmers in the Attested Herds Scheme.

The records of 140 herds which at one time or another participated in the scheme are as under:—

Herds submitted to a preliminary tuberculin test		140
Herds in which no vaccination was done ...	22	
Herds withdrawn before check test	51	
Herds in which a check test was made	67	
	—	140

Reasons for withdrawal of vaccinated herds before check test

Before analysing the results obtained in the vaccinated herds, it is necessary to consider the reason why 51 were withdrawn before the check test was applied. It may here be explained that this test was planned to take place at a time when no tuberculous animals from the original herd remained on the premises and when all the younger stock had been vaccinated with B.C.G. In practice, many owners were unable or unwilling to adhere strictly to this recommendation, so that check tests were sometimes made when unvaccinated, tuberculin-positive animals still remained in the herds.

The reasons for the withdrawal of certain herds were as under:—

Undesirable sequelæ to vaccination	17
Decided to dispose of all reactors forthwith	13
Herd dispersed and replaced with attested stock	1
Labour entailed in vaccination	4
Ceased to rear calves	2
Herd sold	4
No reason recorded	10
	51

Vaccination

No vaccination was carried out in 22 herds. Most of these showed a low incidence of infection, mainly confined to adult stock, at the preliminary test. The owners decided therefore to dispose of all reactors and apply for a T.T. licence. Twenty such herds attained T.T. status early in the trial.

Vaccinations began in the other herds on February 1, 1943, and were ended in November, 1950. In all, 6,725 animals were vaccinated and 30,267 vaccinations were made.

TABLE 2

Table showing Number of Vaccinations per Herd

	Times vaccinated													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Herds withdrawn before check test	9	10	10	7	3	6	2	3	1	0	0	0	0	0
Herds completed to check test	0	0	0	4	8	14	6	10	13	5	4	0	2	1

Undesirable sequelæ to vaccination, whether of a local or of a systemic nature, were recorded in 90 of the 118 vaccinated herds. Of the 51 herds which withdrew from the trial, sequelæ are recorded as the reason for withdrawal of 17. There are, however, records of sequelæ in 37 of these 51 herds. If the herds which were vaccinated only once before withdrawal are excluded, there were 35 herds with recorded sequelæ out of the 42 herds withdrawn.

During the early part of the investigation, no alarming disturbances were reported. In 1943, however, farmers reported illness and lameness in some of the vaccinated animals. At this period, the initial vaccinating dose of B.C.G. was 100 mg. and the reimmunising dose was 50 mg. It appeared that the disturbing effects were mainly confined to those animals to which the larger dose had been given, and it was decided to reduce the inoculum to 50 mg.

Preliminary inquiries by Dr. Jordan indicated that more than one type of reaction was likely to be induced by the vaccine.

Immediate reaction.—This was generally noticed within 24 or 48 hours of vaccination. The temperature rose to 103°—105° F.; the animal was depressed, the appetite was indifferent, the respirations were increased and accompanied by coughing; inco-ordination of movement was not uncommon. Usually these symptoms lasted about 24 hours, after which the animal returned to normal. A number of deaths were reported, however, from acute pulmonary œdema.

Delayed reaction.—This response occurred at any time from 7 to 28 days after vaccination. The first reaction was a rise in temperature which occurred 2 days before obvious symptoms developed. The temperature sometimes reached 104° F. to 105° F. Affected animals were depressed and showed a marked reluctance to rise. They only moved if forced, and then seemed to be very stiff and apparently in pain.

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Inco-ordination of movement was sometimes most marked and, whilst the usual expression was one of dejection, a few cases were met with where the eyes assumed a wild, glazed appearance. A very noticeable and constant feature was the very tucked-up appearance of these animals, which persisted for several days up to a week or two after other symptoms had abated. Trembling, even violent rigors, were sometimes noticed, accompanied by greatly accelerated respirations. Coughing, whilst not often marked, was usually present. Affected animals showed any or all of these symptoms and for 2 to 4 days were very ill. The more violent symptoms never lasted more than 2 or 3 days, and no case terminated fatally. The physical condition of the cattle seemed to have no relation to the probability of an immediate or delayed reaction.

Tuberculin tests

Tuberculin tests, applied at irregular intervals, confirmed the results of the laboratory investigation, indicating that shortly after the intravenous inoculation of a vaccine a highly allergic state developed; this persisted for several weeks and was followed by a gradual decline in sensitivity. Revaccination tended to increase the allergic state.

In the early stages of the investigation, vaccinated animals were tested at fairly regular intervals. Contrary to what was expected, only 8 per cent of the animals tested were reactors four months after vaccination, and the percentage gradually declined to 2 per cent after one year. There was, however, a relatively high proportion of "inconclusive" reactors. The incidence was 32 per cent four months after vaccination, declining to 17 per cent after one year. The preponderance of inconclusive reactions may be explained by the fact that vaccinated animals continue to give indefinite responses to tuberculin for some time. It has also to be remembered that the vaccinated animals were in constant contact with infected non-vaccinated stock belonging to the original dairy stock.

The percentage reacting to avian tuberculin remained fairly constant at about 30 per cent.

It was expected that after vaccination had ceased, the response of vaccinated animals to tuberculin—provided they had not acquired a natural infection—would steadily decline until they eventually became tuberculin-negative. This was, however, not always so, and interpretation was difficult because it is not possible to distinguish the allergy resulting from B.C.G. from that which follows natural infection; this further complicated the difficulties caused by non-specific reactions of the type normally encountered in tuberculin testing.

Throughout the trials, emphasis was laid on the difficulty of interpreting tuberculin tests where large numbers of inconclusive reactors are disclosed in tests after the use of B.C.G., particularly in those animals which have received several doses.

The results of some comparative tuberculin tests using human, bovine, avian and B.C.G. tuberculins in young animals vaccinated once or twice and tested many months after the last dose of vaccine, showed that in most animals

sensitivity to tuberculin faded nine months after the last dose of vaccine, and had disappeared one year after vaccination.

On the usual basis of interpretation, check herd tests carried out within twelve months of the final vaccination resulted in an abnormal number of animals being classed as inconclusive reactors. The reaction to mammalian tuberculin faded in time, and the majority of these inconclusive reactors ultimately passed the test, although a small percentage gave rather persistent reactions.

Check tests

These were completed in respect of 67 herds.

The results (Table 3) were analysed to show the number of reactors and non-reactors in (*a*) vaccinated animals, (*b*) non-vaccinated cows from the original stock still remaining in the herds, and (*c*) non-vaccinated calves born between the cessation of vaccination and the check tests. These figures may be compared with the tuberculous status in the herds revealed by the initial tuberculin tests before vaccination.

The average interval between the last vaccination and check test was just under 11 months, with a range of 4 to 17 months.

TABLE 3

Tuberculin Tests in Vaccinated Herds

PRELIMINARY HERD TESTS

1 Cows			2 Heifers			3 Calves		
No.	R.	%	No.	R.	%	No.	R.	%
2,827	1,847	65.3	2,133	805	37.7	1,005	139	13.8

R. = Reactors

FINAL CHECK TESTS

4 Vaccinated animals			5 Non-vaccinated cows			6 Non-vaccinated calves		
No.	R.	%	No.	R.	%	No.	R.	%
3,637	355	9.8	616	240	30.9	867	35	4.0

R. = Reactors

TABLE 4

Result of Final Check Tests and Status of the Herd

Present status of the herd	Vaccinated			Non-vaccinated calves		
	No.	R.	%	No.	R.	%
Attested	2,271	142	6.2	435	13	3.0
T.T.	759	47	6.1	222	2	1.0
Non-designated	607	166	26.9	208	20	9.6

R. = Reactors

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Attention is drawn to the following points. The incidence of tuberculosis in cows, heifers and calves, as revealed by the preliminary tuberculin test, was very high. At the completion of the vaccination programme there were still a number of herds containing cows belonging to the original stock, and in the latter there was still a high incidence of tuberculosis. This point must be borne in mind when considering the figures for non-vaccinated calves in Column 6, Table 3. Had the owners immediately eliminated all the old stock from their herds when vaccination ceased, the unvaccinated calves would not have been exposed to the same risk of infection. In fact, in many of the herds which became attested or T.T. there was no infection in the calves. The figures in Columns 4 and 6 of Table 3 have been analysed to give the numbers in herds which became attested, or T.T., and those which remained non-designated, respectively. It is perhaps significant that the percentages of reactors amongst the non-vaccinated calves in attested, T.T. and non-designated herds were 3.0, 1.0 and 9.6 per cent respectively (Table 4). These figures are not complete because the information was not available from all the herds.

In regard to the reactions to tuberculin in the vaccinated herds, the percentage figures were: attested herds, 6.2 per cent; T.T., 6.1 per cent; and non-designated, 26.9 per cent. Some of these reactions may have been due to tuberculous infection, but many were undoubtedly attributable to a persistent allergy to the vaccine. A proportion of these animals subsequently passed the test. It was not possible in some herds to identify the vaccinated animals on account of renumbering, and these herds have therefore been omitted.

Post-mortem examinations

Up to the end of 1945, seven animals were examined post-mortem and were free from visible lesions of tuberculosis. In 1946, a further sixteen animals were examined and in two cases lesions of tuberculosis were found.

The first case was a 10-month-old heifer with gross enlargement of the superficial lymphatic glands. Advanced generalised tuberculosis was revealed and the lesions in most organs and lymphatic glands were calcareous. This was possibly a case of pre-vaccination infection.

The second case was a four-year-old cow with an abscess in the retro-pharyngeal lymphatic gland causing stenosis of the pharynx. The post-mortem examination revealed abscesses in the liver and in the retropharyngeal lymphatic glands. The lesions were not typical of tuberculosis and no acid-fast organisms could be demonstrated in smears from the suspected material. Biological examination, however, proved positive for tuberculosis.

In subsequent years it proved impossible to secure further animals for post-mortem examination, and no information is available on the incidence of the disease in vaccinated stock.

Discussion

The effect of isolation and segregation

It is clear that quite early in the trial many owners found vaccination a tedious process and adopted other measures to hasten attainment of their goal

of a T.T. herd. It was perhaps asking too much of a progressive farmer whose herd had been submitted to a tuberculin test to expect him not to distinguish between reactors and non-reactors when culling. As from October 1, 1943, the payment of a quality premium of 4d. per gallon on all milk sold from licensed T.T. herds was commenced. There is no doubt that this added inducement to owners to expedite the removal of reactors from their herds had a marked influence. Considering only those herds which remained in the trial, there is good reason to believe that an appreciable number of reactors were disposed of in this way.

Apart from the removal of reactors from the farms, the results were also influenced to a marked degree by the segregation of vaccinated and non-vaccinated animals. Several definite cases of segregation are recorded and in farms with more than one milking shed, as is common in the Home Counties, it would be a simple matter, and a great temptation, to house reactors and non-reactors separately pending the disposal of the former. The net result of the foregoing suggests that in many herds newly calved heifers on entering the milking herd were not exposed to anything like the weight of infection they would have encountered in other circumstances. Nor in many cases were they exposed to potential infection for the time that had been expected. Many owners, with the object of applying for a T.T. licence, requested that vaccination should cease in order that a herd test might be carried out.

The summary shows that at the dates of the check tests some 40 per cent of the herds still contained an appreciable number of original non-vaccinated animals. In other cases the owners had removed the non-vaccinated group, or the known reactors from this group, just before the check test.

Control herds

In view of the absence of adequate controls, an attempt has been made to study the comparative speed with which a herd may be cleaned of infection without the use of vaccine. Information has therefore been extracted from the

TABLE 5

		No. attested or supervised before Jan. 15, 1952	Herds containing only a total of 3 reactors at last test	Proceeding later under Article 6*	Owners giving up farming	No progress made or forecast
No. of herds	...	113	73	9	14	4	13
Cattle	... ...	6,153	3,967	430	795	174	787
Reactors	... ...	2,412	1,448	151	401	103	309
Reactors, per cent		39.2	36.5	35.1	54.4	59	39.3
Cows	... ...	2,540	1,687	133	331	76	313
Reactors	... ...	1,752	1,143	82	247	63	217
Reactors, per cent		69.0	67.7	61.6	74.6	84	69.3

* The Tuberculosis (Attested Herds) Scheme, 1950. Under this provision all cattle in heavily infected groups are removed at once, and after disinfection of the premises, etc., are replaced by attested stock.

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papers concerning herds in the area in South-west Scotland where free testing is being done under the tuberculosis area eradication plan. The first test recorded is not necessarily the first test of the herd, but it is the first of which we have any record. Herds were selected for this record on three conditions: (1) that they contained 25 or more cattle; (2) that at least 20 per cent of the animals reacted at the first test of which the detailed result is available; and (3) that the first test was made between October 1, 1950, and April 30, 1951.

The data give no indication of the comparative cost of the two methods but they do show the time taken to eliminate infection.

Of the 113 herds recorded, 71 became attested or supervised within a year of the first test. Details are shown in Table 5.

Effects of vaccination

There is no doubt that vaccination proved successful in those herds in which the calves were not exposed to infection until the immunity following the first vaccination had developed. There are, however, certain drawbacks to the use of B.C.G. under field conditions.

Owners in general found the trial tedious. The labour entailed in repeated vaccinations is considerable, especially as one of the biannual vaccinations has to be done during the summer season when young stock may be grazing a long way from the farmstead or, as is not uncommon, on detached pastures. It is apparent from the records that the more progressive farmers were those who terminated the trial prematurely.

Many owners reported systemic reactions following vaccination. In some animals the symptoms observed were so slight and transient as to be hardly noticeable. In others they were severe and persistent, and in a few others death occurred within hours of inoculation. In the light of experience many owners refused to permit vaccination of cows at the height of their lactation on the ground that where severe systemic reactions occurred milk production dropped sharply. They asserted that although the milk yield recovered to a considerable extent within a few days it never returned to normal. This opinion is not borne out by recorded trial observations but is supported to some degree by the sequence of events following other temporary upsets of lactating cows where a recession in milk yield is seldom followed by complete return to normal production levels.

On some farms vaccination of young stock sometimes caused prolonged and severe systemic reactions which may have initiated such a check in growth as to result in stunting. It is important to note that these only occurred where young stock were maintained at a very low level of nutrition. Such conditions were frequently found on the holdings of the less progressive farmers and were especially common during the war years.

Experience in the trial showed the necessity for definite identification of stock and the maintenance of accurate records. It is obvious that owners could not be relied upon to keep such records and that without outside supervision individual herd records would soon have become chaotic. It is difficult to

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determine from this field trial how far B.C.G. was effective in eliminating tuberculosis from heavily infected herds. There is no doubt that a substantial reduction in the disease was secured without seriously interfering with herd management, but it is arguable that equally satisfactory results might have been achieved by other means. The information which it was hoped to obtain from the controlled unvaccinated herds is not sufficiently detailed to give an answer to this point.

Of the 67 herds in which the full vaccination programme was completed and check tuberculin tests were carried out, 37 became attested, 14 obtained a T.T. licence. In 16 there was little or no progress towards eradication of tuberculosis. It is not possible, for a variety of reasons mentioned in the report, to attribute these results solely to the use of B.C.G. In many cases the owners who participated in the scheme soon became far more conscious of the drawbacks of retaining tuberculous animals, and took other steps to eliminate infection, but it is highly probable that the success was at any rate partly due to the vaccine. In general, the vaccinated animals, as judged by the final tuberculin tests, have resisted exposure to infection the weight of which varied in the different herds, and was in any case a diminishing factor.

If it can be assumed that B.C.G. has some value, it is necessary to put into the balance on one hand the considerable cost under the Attested Herds Scheme of eliminating tuberculin-positive animals or even the replacement of a whole herd by fresh attested stock, with the immediate benefit of tubercle-free animals; and on the other hand the slower progress which is obtained with B.C.G. coupled with the expense of repeated vaccination and the danger of occasional deaths or temporary loss of condition in vaccinated animals.

Summary

1. Two field trials on the value of B.C.G. in controlling tuberculous infection in heavily infected herds have been completed.

2. In the West Sussex investigation 47 calves vaccinated by the intravenous route were placed on four farms in which animals were being removed under the Tuberculosis Order. The trials began in 1935 and ended in 1944. The animals were revaccinated at six-monthly intervals. The original plan of subjecting to post-mortem examination all the vaccinated animals together with an adequate number of non-vaccinated controls of the same age and kept under similar conditions could not be completed, partly because of changes in ownership and other factors on the farms, and partly owing to the difficulty of following up the animals under war-time conditions.

Of the 33 animals which were examined post-mortem, confirmation of the presence or absence of tuberculosis by the inoculation of guinea-pigs with suitable tissues was obtained in 21; 4 were tuberculous and 17 were free from infection. In the remaining 12, in which the nature and extent of the lesions was judged by naked eye only, 5 were tuberculous and 7 were not infected. On the whole, the tuberculous lesions in vaccinated animals were not extensive.

No in-contact control animals were examined post-mortem. Nevertheless,

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the incidence of tuberculosis in the herds, as judged by tuberculin tests and the seizure of the animals under the Tuberculosis Order, remained high throughout the trials and the vaccinated stock would appear to have been exposed to heavy contact infection.

3. In the Berkshire experiment 140 herds participated in the trial which began in 1943; 22 were withdrawn at an early stage, 51 continued in the scheme for varying periods between 1943 and 1949, and 67 were retained until the objects of the investigation were completed.

The herds were all heavily infected with tuberculosis at the commencement of the trial. Tuberculin-negative calves were vaccinated intravenously with B.C.G. when three to six months of age; older animals were included if they were not reactors to tuberculin. Revaccination was carried out at six-monthly intervals. At a later stage, when most or all of the original tuberculin-positive animals had been removed, vaccination ceased and a check tuberculin test was applied.

The number of animals subjected to post-mortem examination was too small to yield any evidence of value on the efficacy of the vaccine. The results of check tuberculin tests in the 67 herds in which the programme was completed were as follows: 37 became attested, 14 obtained T.T. licences, and in 16 there was little or no progress towards eradication of tuberculosis.

4. Details are given of reactions to the vaccine which were encountered in 32 of the herds. In 3 animals which succumbed, death was attributed to the vaccine. In other cases B.C.G. produced signs of shock immediately after administration or about three to four weeks later. The symptoms were severe in some cases but mild in others.

5. In the early stages the vaccinated animals became negative to tuberculin after a few months and usually before they were revaccinated. The check tuberculin tests carried out at the end of the trial were more difficult to interpret owing to an apparent persistence of indefinite reactions in a proportion of the vaccinated stock, although eventually most of these passed the test.

Acknowledgments

The Committee is greatly indebted to its former Chairman, Sir T. Dalling, for his constant advice and encouragement.

Thanks are also due to Mr. Salter Chalker, the representative of the N.F.U., and to those farmers who placed their herds at the disposal of the Committee; to Superintending and Divisional Inspectors of the Ministry's Animal Health Division, and the veterinary practitioners who helped to recruit farmers for the Berkshire trials and were responsible for some of the tuberculin tests; and to the Ministry staff at the Veterinary Laboratory, Weybridge, who prepared the vaccine and carried out some of the post-mortem examinations.

Special investigations were undertaken by Dr. Blaxter on stunting associated with B.C.G., and by Dr. H. H. Holman, M.R.C.V.S., A.R.C. Field Station, Compton, on anaphylaxis.

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REFERENCES

Ascoli, A. (1927): *Ann. Inst. Pasteur, 41,* 314; (1930) 11th *Internat. Vet. Cong.*; (1931) *Ann. Inst. Pasteur, 47,* 29; (1932) *Rec. Tuberc., 13,* 5; (1937) "Esperimenti di Vaccinazione Anti-tubercolari." Figli: Milan.
Bang, O., Jundell, I., and Magnusson, H. (1931): *Ann. Inst. Pasteur, 49,* 630.
Brunzema and Kauffmann (1933): *Zeitschr. Hyg. Infektkr., 115,* 370.
Buxton, J. B., and Griffith, A. S. (1931): *Lancet, 220,* 393.
Buxton, J. B., Glover, R. E., and Griffith, A. S. (1934): *Rept. Inst. Anim. Path., 4,* 262.
Buxton, J. B., Glover, R. E., Dalling, T., and Bosworth, T. J. (1939): *J. comp. Path., 52,* 272.
Calmette, A., and Guérin, C. (1920): *Ann. Inst. Pasteur, 34,* 553; (1924) *Ibid., 38,* 371; (1928) *Ibid., 42,* 175.
Cotton, W. E., and Crawford, A. B. (1932): *J. Amer. vet. med. Ass., 80,* 18.
Gerlach, F. (1929): *Rev. Gén. méd. Vét., 38,* 392; (1931) *Ann. Inst. Pasteur, 47,* 475; (1932) *Wien. tierarzt. Wschr., 14,* 353.
Griffith, A. S., Buxton, J. B., and Glover, R. E. (1931): *Rept. Inst. Anim. Path., Camb., 2,* 46.
Guérin, C. (1933): *Rév. méd. vét., 109,* 5.
Guérin, C., Richart, A., and Boissière, M. (1927): *Ann. Inst. Pasteur, 41,* 233.
Haring, C. M., Traum, J., Hayes, F. M., and Henry, B. S. (1930): *Hilgardia, 4,* No. 12.
Irvine, K. N. (1949): "B.C.G. Vaccination in Theory and Practice." Blackwell: Oxford.
Jundell, I., and Magnusson, H. (1933): *Svensk. Vet. tidskr., 38,* 391, abstracted in *Vet. Bull.* (1934), *4,* 413.
King, M. J. (1929): *Cornell Vet., 19,* 96.
Lange, B. (1930a): *Dtsch. med. Wschr., 56,* 927; (1930b) *Zeitschr. f. Tuberk., 59,* 1.
Lange, B., and Wethmar, R. (1929): *Zeit. f. Tuberk., 110,* 465.
Petroff, S. A., Branch, A., and Steenken, W. (1929): *Amer. Rev. Tuber., 19,* 9.
Rankin, C. (1929): *Ann. Inst. Pasteur, 43,* 878.
Rankin, A. C., Ower, J. J., Shaw, R. M., Talbot, P. S., and Vango, H. M. (1932): *Canad. J. Res., 6,* 177.
Schroeder, E. C., and Crawford, A. B. (1929): *J. Amer. vet. med. Ass., 74,* 772.
Tzechnovitzer, M. (1927): *Ann. Inst. Pasteur, 34,* 553; (1928) *Ibid., 42,* 246; (1930) *Ibid., 45,* 162.
Watson, E. A. (1930): *11th Internat. Vet. Cong.*; (1933) *Canad. J. Res., 9,* 1928; (1934) *12th Internat. Vet. Cong., 2,* 2.
Watson, E. A., McIntosh, S. W., and Konst, H. (1928): *J. Amer. vet. med. Ass., 73,* 799.

THE BLOOD AND NERVE SUPPLY TO THE MAMMARY GLANDS OF THE CAT, AND OTHER LABORATORY ANIMALS

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THE present work was carried out in connection with a study of the vasomotor nerves to the mammary glands since insufficient anatomical data for the species studied were obtainable in the literature. Most attention has been given to the cat and the other species studied only in so far as they correspond with or differ from this animal.

The anatomical texts of Mivart (1881), Reighard and Jennings (1925, 1951) for the cat, and Krause (1868) and Gerhardt (1909) for the rabbit make no reference to the blood and nerve supply to the mammary glands. Those of Greene (1935) for the rat, and Sisson (1940), Ellenberger and Baum (1943),

* Work partly carried out in the Department of Physiology, University of Edinburgh.

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Terminology used by various author compare

DOG					CAT		
Miller (1948)	Bradley (1948)	Ellen-berger and Baum (1943)	Sisson (1940)	Turner (1939)	Mivart (1881)	Reighard and Jennings (1925)	Turner (1939)
BLOOD VESSELS							
Internal thoracic	Internal thoracic	Internal thoracic	Internal thoracic	Internal thoracic	Internal mammary	Internal mammary	Internal mammary
Cranial epigastric	Cranial epigastric	Cranial epigastric	Anterior abdominal	Anterior abdominal	—	—	—
Cranial superficial epigastric	—	—	—	Anterior abdominal	—	—	Anterior or ext. mammary
Lateral thoracic	External thoracic	External thoracic	External thoracic	—	Long thoracic	Long thoracic	—
Phrenico-abdominal	Phrenico-abdominal	Phrenico-abdominal	Phrenico-abdominal	—	Supra-renal	Adreno-lumbar	—
Deep circumflex iliac	Deep circumflex iliac	Deep circumflex iliac	Circum-flex iliac	—	—	Ilio-lumbar	—
External pudendal	External pudendal	External pudendal	External† pudic	External pudic	—	External spermatic	—
Caudal superficial epigastric	—	Caudal mammary	Subcut. abdominal	Posterior mammary	—	—	Posterior mammary or epigas-tric
Superficial cervical	—	—	—	—	—	Anterior thoracic	—
Caudal epigastric	Caudal epigastric	Caudal epigastric	Posterior abdominal	—	Epigastric	—	Hypo-gastric ?

† Mammary artery is branch of it in female

NERVES							
External spermatic	External spermatic	External spermatic	External spermatic	—	Genito-aural	Medial branch genito-femoral	—
Lateral thoracic	Pectoral	Lateral‡ thoracic	External thoracic	—	—	Anterior thoracic	—
Lateral cutaneous femoral	Lateral cutaneous femoral	Lateral cutaneous femoral	Lateral cutaneous femoral	—	Ilio-inguinal ?	—	—

‡ or thoraco-ventralis

compared with that used in the text.

Turner (1939)	RABBIT Krause (1868)	RABBIT Gerhardt (1909)	RABBIT Wahl (1915) Turner (1939)	RAT Greene (1931)	MOUSE Turner (1939)	GUINEA PIG Turner (1939)
Internal mammary	Internal mammary	Internal mammary	Internal mammary	Internal mammary	Internal mammary	—
—	Superior epigastric	Superior epigastric	Epigastric	Superior epigastric	Epigastric	—
Anterior or ext. mammary	—	—	—	—	—	—
—	Long thoracic	Long thoracic	Thoraco-epigastric or ext. mam.	Lat. thoracic	Thoraco-epigastric or ext. mam.	—
—	Lateral* abdominal	(off renal)	—	Long. „ Ext. mam. Supra-renal	—	—
—	—	—	—	Ilio-lumbar	—	—
—	External spermatic	External spermatic	—	Pudic-epigastric trunk	—	Superficial epigastric
Posterior mammary or epigastric	—	—	Superficial epigastric	—	Superficial epigastric	—
—	Superficial cervical	Superficial cervical	—	Superficial cervical	—	—
Hypogastric ?	Inferior epigastric	Inferior epigastric	—	Pudic-epigastric trunk	Hypogastric ?	Hypogastric ?

*12th intercostal off renal as well

—	External spermatic	External spermatic	—	External spermatic
—	Long* pectoral	Long pectoral	—	Lateral thoracic
—	Lateral cutaneous femoral	Lateral cutaneous femoral	—	Lateral cutaneous femoral
	Supra-clavicular	Supra-clavicular	—	Middle supra-clavicular

*Running with abdominal vein

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Bradley (1948) and Miller (1948) for the dog give the major blood vessels supplying the mammæ, the most complete being the accounts of Miller and Greene. Similar information is given for the dog and cat by Turner and Gomez (1934) and Turner and de Moss (1934), for the rabbit by Wahl (1915) and for all the domesticated animals in the monograph by Turner (1939).

Of the authors named only Ellenberger and Baum (1943) and Miller (1948) give any information on the gross nerve supply to the mammary glands of these laboratory mammals.

Unfortunately the literature shows no uniformity of nomenclature, and several vessels and nerves to be described have not been mentioned before in anatomical texts dealing with the particular species. The I.N.A. system used by Miller (1948) has been followed in this paper because he is the only author to name all the vessels encountered. The alternative names that have been used by other authors are given in an Addendum.

Animals and Methods

Detailed dissections were made of the blood vessels and nerves supplying the lactating mammary glands of six dogs, seventeen cats, six rabbits, four guinea-pigs, three rats and five mice. The recognition of smaller vessels was facilitated in the majority of cases by the injection of Indian ink or coloured solutions of neoprene latex (I.C.I.) or gelatin. The neoprene injected specimens (two dogs, three cats) were completely macerated after dissection for the confirmation and detection of anastomoses between the larger vessels.

The areas of skin supplied by the lateral cutaneous branches of the lumbar and some thoracic spinal nerves were determined in six female cats (five under anæsthesia, one decerebrate). Electrodes were placed under the uncut nerves and the action potentials produced by stroking the hairs of the innervated areas were picked up, amplified and recorded with an oscillograph and loudspeaker. By this method the dermatome of each nerve could be quickly determined and plotted.

Cat and Dog

In the lactating state the mammary glands in these species form a continuous band of tissue running from the axilla to the inguinal region, between the skin and the panniculus carnosus muscle. (The cat normally has four pairs of glands and the dog four to six.) There is an extensive network of large arteries and veins permeating the mammary tissue, supplied from three main sources:—

(*a*) Caudally the caudal superficial epigastric artery and vein which originate from the external pudendal vessels in the inguinal canal, and pass forward on the dorsolateral aspect of the abdominal glands to join—

(*b*) The cranial superficial epigastric vessels, which emerge through the abdominal wall just behind the xiphoid cartilage in the midline and originate from the internal thoracic vessels.

(*c*) The lateral (or external) thoracic vessels, originating from the axillary vessels, travel caudally on the lateral edge of glands 1 and 2, to which they supply branches. These vessels are smaller than (*a*) and (*b*).

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In addition to these main vessels there are, in order of size:—

(*d*) Several branches (two to four) from the internal thoracic vessels, which pass between the costal cartilages near the sternum, to enter the first pair of glands medially.

(*e*) A series of parallel vessels running ventrolaterally around the body beneath the panniculus carnosus muscle in company with the lateral cutaneous thoracic and lumbar nerves, to anastomose with the caudal superficial epigastric and lateral thoracic vessels. The vessels travelling with the lateral cutaneous femoral nerve (L IV) arise from the deep circumflex iliac vessels, those with nerves from L I, II and III from the phrenico-abdominal vessels, and the rest from the intercostal vessels. The latter usually extend as far forward as T VII, but branches from T VIII or IX are sometimes missing.

(*f*) A few small twigs from the epigastric vessels within the abdominal wall passing through it to enter glands 3 and 4 dorsally.

(*g*) A variable number of vessels (often only veins) crossing the midline between glands 3 and 4.

A valve is usually present in the external pudendal vein just outside the inguinal canal. This was the only valve encountered in the mammary veins.

The nerve supply is also multiple. The lateral cutaneous branches of the ventral divisions of the thoracic and lumbar spinal nerves enter the glands laterally, from T III to L III inclusive. T II does not send macroscopically visible fibres to the first gland and L IV (lateral cutaneous femoral nerve) has medial branches which enter the inguinal fat but which cannot usually be seen entering the inguinal mammary gland with the naked eye, although physiological evidence was obtained that vasoconstrictor fibres in this nerve may reach the inguinal gland (Linzell, 1950). The inguinal gland receives in addition most of its vasomotor innervation from the external spermatic nerve, reaching it in company with caudal superficial epigastric vessels from the inguinal canal. The ventral cutaneous branches of the intercostal nerves, which emerge through the interchondral spaces, in company with vessels from the internal thoracic artery and vein, also send some branches to the thoracic glands. A few small nerves have also occasionally been found entering glands 3 and 4 on the dorsal aspect from the overlying abdominal wall. These originate from the muscular branches of the ventral spinal nerves supplying the abdominal muscles.

The lateral thoracic nerve, which accompanies the vessels of the same name along the lateral edges of glands 1 and 2, does not, as far as can be seen, send any branches to the mammary glands, although it apparently sometimes anastomoses with the lateral cutaneous nerves travelling across it. It has been shown to innervate the panniculus muscle in the dog and cat (Langworthy, 1924) and the Achselbogen muscle (Wilson, 1913), which is the homologue of the panniculus in man. Stimulation of the nerve caused contraction of the panniculus muscle; that of the lateral cutaneous nerves did not.

Rabbit

The rabbit has three to five pairs of mammary glands arranged as in the dog and cat. The caudal superficial epigastric vessels do not come from the

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external pudendal vessels however, but leave the femoral vessel in the thigh, and anastomose with the external pudendals within the inguinal gland. The lateral thoracic vessels are relatively larger than in the dog and cat, and appear to play a greater part in supplying the cranial glands over the thorax than the vessels from the internal thoracics. The vessels which exactly correspond in origin and position to the deep circumflex iliacs in the cat and dog are called the iliolumbar by Krause (1868) and Gerhardt (1909). They are also relatively larger and anastomose with the caudal superficial epigastrics and the subscapular vessels. Superficial extensions of the latter are very prominent in this species, and also join the lateral thoracic vessels. In addition gland 1 receives a pair of vessels not present in the cat and dog. These arise either from the axillary (emerging just behind the clavicle) or less commonly from the subclavians in front of the clavicle (superficial cervical). They are accompanied by a superficial nerve from C IV. The phrenico-abdominal vessels supplying lateral cutaneous branches to the abdominal and inguinal glands are called the lateral abdominal by Krause (1868).

Rat and Mouse

In these species the glands are arranged in two groups around the axilla (three pairs) and inguinal region (three pairs in the rat and two pairs in the mouse), so that the middle region of the abdomen is devoid of glands. Unlike the cat, dog and rabbit, the mammary glands of the rat and mouse lie beneath the panniculus carnosus muscle and not between it and the skin. The blood and nerve supply more resemble the rabbit than the dog and cat. However, there is no vessel corresponding to the cranial superficial epigastrics of the other species and this area of the abdominal skin is supplied by a branch of the lateral thoracic. The anastomosis between the caudal superficial epigastric and the external pudendal is less conspicuous than in the rabbit.

The subscapular vessels are not prominent.

Guinea-pig

The guinea-pig has only two mammary glands situated in the inguinal region, and the blood is supplied almost entirely by the external pudendal vessels, some branches of which extend beyond the glands anteriorly. Some very small branches also reach the glands from vessels which correspond to the caudal superficial epigastrics of the rabbit, rat and mouse.

The external spermatic nerve sends two large branches to the gland. One accompanies the external pudendal vessels as in the other species, but the other leaves the abdominal cavity laterally above the inguinal ligament and enters the gland a little way in front of the other vessels and nerves.

The posterior part of the gland is drained by an additional vein (unaccompanied by an artery) which joins the perineal branch of the external pudendal vein.

Anomalous Findings

In seven of 102 cats examined an additional large vein was present joining

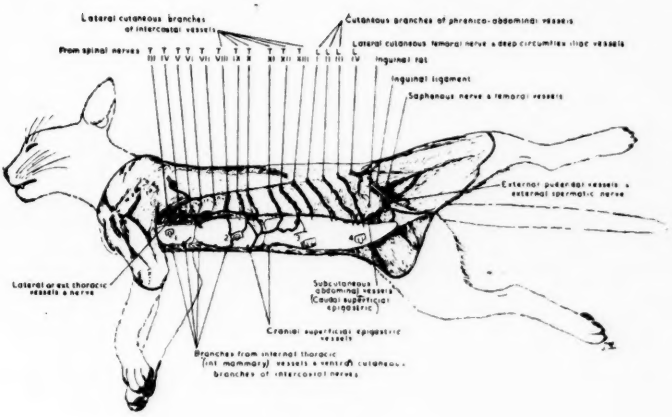
Lateral cutaneous branches of intercostal vessels
Cutaneous branches of phrenico-abdominal vessels
From spinal nerves
Lateral cutaneous femoral nerve & deep circumflex iliac vessels
Inguinal rat
Inguinal ligament
Saphenous nerve & femoral vessels
External pudendal vessels & external spermatic nerve
Lateral or ext thoracic vessels & nerve
Subcutaneous abdominal vessels (Caudal superficial epigastric)
Cranial superficial epigastric vessels
Branches from internal thoracic (int mammary) vessels & ventral cutaneous branches of intercostal nerves

Fig. 1.
Drawing of the blood and nerve supply to the mammary glands of a lactating cat.

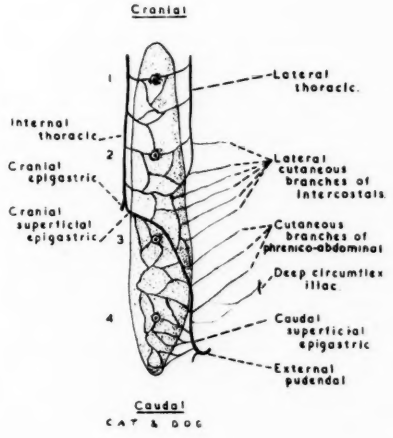

Fig. 2.
Diagram of the arterial supply to the mammary glands of the cat and dog. The veins are similar.

(Article by Linzell, page 427)

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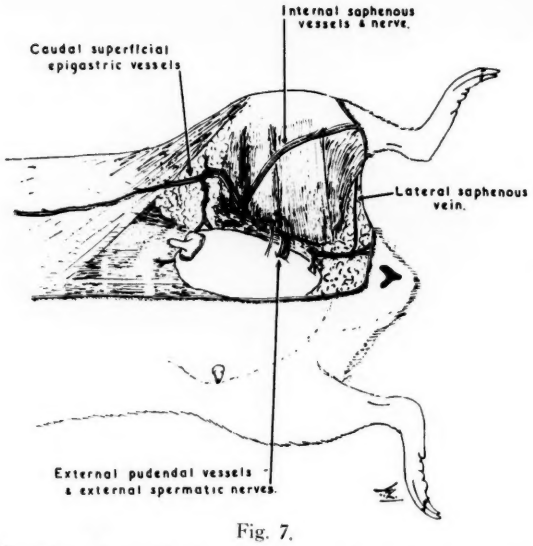
Internal saphenous vessels & nerve.
Caudal superficial epigastric vessels
Lateral saphenous vein.
External pudendal vessels & external spermatic nerves.

Fig. 7.
Drawing of the blood and nerve supply to the mammary gland of a lactating guinea-pig.

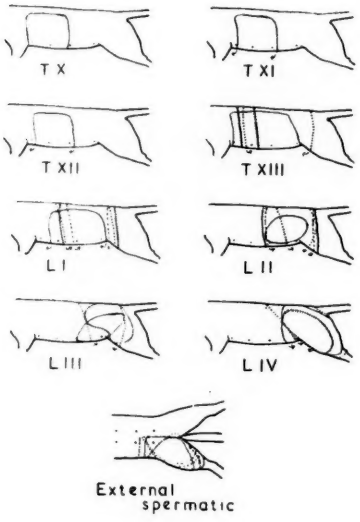

Fig. 8.
Diagram of skin areas supplied by the lateral cutaneous branches of the spinal nerves in six female cats.

(Article by Linzell, page 427)

the caudal superficial epigastric to the femoral vein low in the thigh. In two cases the condition was bilateral, in one case on the left side, and the rest on the right. In three animals the right external pudendal vein was double as well. This anomaly is of interest as this form of venous drainage of the posterior glands is found normally in the rabbit, rat and mouse, and suggests that this more complicated system has been lost by the cat.

Dermatomes

For physiological purposes it was necessary to know the approximate areas of mammary tissue supplied with vasomotor fibres by the different spinal nerves. Since Bellini (1948) has shown that the sympathetic fibres and sensory fibres in spinal nerves supply approximately the same areas in the cat, the sensory dermatomes covering the abdominal and inguinal glands were plotted by the method described. The results shown in Fig. 8 indicate that any one area is innervated by at least five adjacent nerves and that there is considerable variation from cat to cat and even on the two sides of the same animal. Later physiological experiments showed that the inguinal gland received vasomotor constrictor fibres from nerves T XIII to L IV (i.e., the same as sensory innervation) and thus confirmed Bellini's findings (Linzell, 1950).

Acknowledgments

I am grateful to S. D. Carlill for assisting me with the electrical apparatus used for plotting the sensory dermatomes.

REFERENCES

Bellini, E. (1948): "Innervazione spinale ed innervazione simpatica della cute: rapporti topografici." *Sperimentale, 99,* 42.

Bradley, O. C. (1948): "Topographical Anatomy of the Dog." 5th ed. Edinburgh: Oliver and Boyd.

Ellenberger, W., and Baum, H. (1943): "Handbuch der Vergleichenden Anatomie der Haustiere." 18e Aufl. Berlin: Julius Springer.

Gerhardt, U. (1909): "Das Kaninchen." Leipzig: W. Klinkhardt.

Greene, E. C. (1935): "The Anatomy of the Rat." Philadelphia: *Proc. Amer. Phil. Soc., 27.*

Krause, W. (1868): "Die Anatomie des Kaninchens in topographischer und operativer rucksicht." Leipzig: W. Englemann.

Langworthy, O. R. (1924): "The Panniculus Carnosus in Cat and Dog and its Genetical Relation to the Pectoral Musculature." *J. Mammol., 5,* 49.

Linzell, J. L. (1950): "Vasomotor Nerve Fibres to the Mammary Glands of the Cat and Dog." *Quart. J. exp. Physiol., 35,* 295.

Lim Boon Keng (1893): "On the Nervous Supply of the Dog's Heart." *J. Physiol., 14,* 467.

Miller, M. E. (1948): "Guide to the Dissection of the Dog." 2nd ed. Ithaca, N.Y.

Mivart, St. G. (1881): "The Cat—an Introduction to the Study of Backboned Animals, especially Mammals." London: John Murray.

Reighard, J., and Jennings, H. S. (1925, 1951): "Anatomy of the Cat." 2nd ed., 1925; 3rd ed., 1951. New York: Henry Holt & Co.

Sisson, S. (1940): "Anatomy of the Domestic Animals." 3rd ed. Philadelphia: W. B. Saunders.

Turner, C. W. (1939): "The Comparative Anatomy of the Mammary Glands, with Special Reference to the Udder of Cattle." Columbia, Missouri: Univ. Co-op. Store.

Turner, C. W., and Gomez, E. T. (1934): "The Normal and Experimental Development of the Mammary Gland. II—The Male and Female Dog." *Mo. agr. exp. Sta. Res. Bull., 207.*

Turner, C. W., and de Moss, W. R. (1934): "The Normal and Experimental Development of the Mammary Gland. I—The Male and Female Domestic Cat." *Mo. agr. exp. Sta. Res. Bull., 207.*

Wahl, H. M. (1915): "Development of the Blood Vessels of the Mammary Gland in the Rabbit." *Amer. J. Anat., 18,* 515.

Wilson, J. T. (1913): "The Innervation of the Achselbogen Muscle." *J. Anat., Lond., 47,* 8.

XUM

THE EFFECT OF ADRENOCORTICOTROPHIC HORMONE AND ADRENAL CORTICAL EXTRACT ON THE DIFFERENTIAL WHITE CELL COUNT IN THE PIG

By D. LUKE, Ph.D., B.Sc., M.R.C.V.S.
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PARTICULAR attention has been paid in recent years to the defensive mechanisms of the body especially to the changes in the numerical relationships of the white blood corpuscles which accompany the responses of the body to a variety of stimuli. Special attention has been drawn to the lymphopenia seen in many immunological phenomena and knowledge has been gained as to the role of the lymphocyte in many of these reactions, as well as insight into the mechanism whereby some at least of these are initiated. The work of McMaster and Hudack (1935), Ehrich and Harris (1942) and Dougherty and White (1944) emphasised the close association between the lymphocyte and antibody formation while White and Dougherty (1946) showed that the dissolution of the lymphocytes was regulated by the pituitary-adrenal cortical secretion.

The effect in the blood picture of pigs injected with adrenocorticotrophic hormone and adrenal cortical extract has been studied. In the normal pig, the number of neutrophils is always lower than that of the lymphocytes; of 110 blood samples taken from normal pigs of various ages the average count was: Total white cells 19,866, neutrophils 6,363 (32 per cent), lymphocytes 13,076 (66.4 per cent) and eosinophils 327 (1.7 per cent). Two preparations were used in the present experiments: (a) Cortisone acetate prepared by Merck and Company which consists of 11-dihydro-17-hydroxycorticosterone-21-acetate and is one of a series of crystalline preparations isolated from extracts of the adrenal cortex of animals; (b) the adrenocorticotrophic hormone prepared by Armour and Company from an extract of the anterior pituitary gland of animals, this is said to stimulate the adrenal gland to secrete cortical hormones.

In order to obtain some information as to the probable effective dosage rates two pigs weighing 120 and 115 lb. were given 300 and 200 mg. respectively of cortical extract. Differential blood counts were made every two hours during a 12-hour period after administration. In the pig receiving 300 mg. there were no significant changes in the numerical relationship between the lymphocytes and the neutrophils. In the second pig a transient depression occurred in the number of lymphocytes within two hours. In both cases there was a slight increase in the number of eosinophils eight hours after injection. The results were disappointing in view of the amounts of the drugs used. It was decided to investigate further using younger pigs. Two pigs weighing 50 lb. and 40 lb. were given 500 mg. of cortisone and 25 mg. of adrenocorticotrophic hormone. It was hoped that the large dose of extract would elicit a clear-cut reaction and that the dose of the hormone would give some indication of the activity of this preparation in the young pig.

The results of the large dose of cortical extract are depicted in Fig. 1. In

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the total white cell count there was an initial drop followed by a sharp increase which was at its peak at 26 hours. Thereafter there was a steep drop up to 50 hours, then a second rise up to 74 hours and a return to normal levels by 98 hours. In this pig there was an absolute lymphopenia established at two hours,

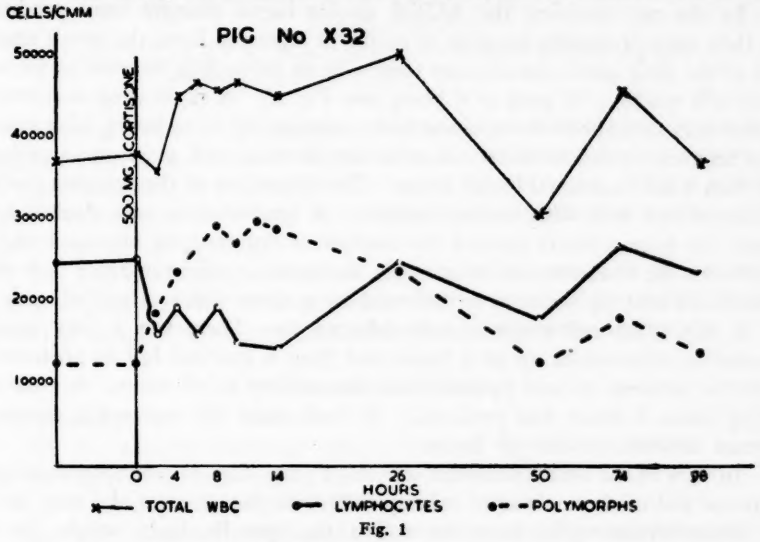

Fig. 1

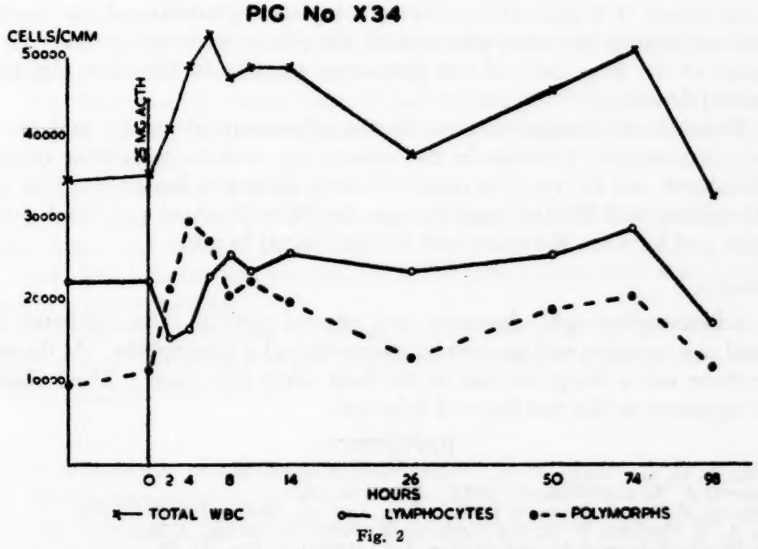

Fig. 2

the lymphocyte level remained low with slight fluctuations up to 14 hours; a slight increase took place between 14 and 26 hours. A secondary drop followed between 26 and 50 hours and normal values were re-established by 74 hours.

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There was an increase in neutrophils which reached its peak between 4 and 8 hours. Thereafter there was a steady drop to normal levels by 50 hours. These changes produced a cross-over in the lymphocyte neutrophil ratio which lasted just under 26 hours.

In the pig receiving the ACTH similar blood changes were produced, but they were of shorter duration as might be expected from the much smaller dose of the drug used. In this case there was an immediate increase in the total white cells reaching its peak at 6 hours (see Fig. 2). A slight drop occurred by 8 hours and then the level remained fairly constant up to 14 hours, with a sharp drop between 14 and 26 hours. A secondary increase took place up to 74 hours and then a fall to normal by 98 hours. The behaviour of the lymphocytes was similar to that seen with cortical extract. A lymphopenia was marked by 2 hours, but from 4 hours onward the number of lymphocytes increased and by 8-10 hours the level returned to normal. A secondary slight increase took place between 26 and 74 hours to be followed by a drop which coincided with the fall in the white cell count already referred to. There was a very marked increase in neutrophils up to 4 hours and then a gradual fall to 26 hours, a slight rise between 26 and 74 hours and then a drop to 98 hours. A cross-over lasting about 6 hours was produced. In both cases the eosinophils tended to increase between 50 and 98 hours.

In view of the results obtained with the 25 mg. dose of adrenocorticotrophic hormone and of those obtained subsequently with dosage rates of 1 mg. per lb. for adrenocorticotrophic hormone and 2 mg. per lb. body weight for the cortical extract it is difficult to offer an adequate explanation of the negative results obtained in the older pigs used in the pilot experiment outlined above. Supplies of the drug used did not permit the response in the older pigs to be examined further.

These blood changes induced by the adrenocortical extract and by the adrenocorticotrophic hormone in the younger pig conform with those reported by Reinhardt and Li (1945) in rats, by Yoffey, Reiss and Baxter (1946) in cats, by Dougherty and White (1942) in mice, by Hills, Forsham and Finch (1948) in man, and by Kerr, Robertson and McGirr (1951) in cattle.

Summary.

Adrenocorticotrophic hormone and adrenal cortical extract injected into normal pigs caused a well marked lymphopenia and a neutrophilia. At the same time there was a sharp increase in the total white cell count. These changes were apparent within two hours of injection.

REFERENCES

Ehrich, W. G., and Harris, T. N. (1942): *J. exp. Med. 76,* 335.
Dougherty, F. T., and White, A. (1942): *Science 98,* 367.
Dougherty, F. T., and White, A. (1944): *Proc. Soc. exp. Biol. and Med. 57,* 295.
Hills, A. G., Forsham, P. H., and Finch, C. A. (1948): *J. Hæmat., 3,* 755.
Kerr, W. R., Robertson, M., and McGirr, J. L. (1951): *J. Hyg. 49,* 67.
McMaster, P. D., and Hudack, S. S. (1935): *J. exp. Med. 61,* 783.
Reinhardt, W. O., and Li, C. H. (1945): *Science. 101,* 360.
White, A., and Dougherty, F. T. (1946): *Ann. N.Y. Acad. Sci. 46,* 679.
Yoffey, J. M., Reiss, M., and Baxter, J. S. (1946): *Nature 157,* 368.

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CHLORAL HYDRATE, ANÆSTHESIA AND TOXICITY IN DOGS

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CHLORAL hydrate has long been used as a general anæsthetic for the horse. Kaufmann (cited in Hobday's Surgical Diseases of the dog and cat) stated that the anæsthetic dose of chloral hydrate for the dog is 4 gm. It was stated by British practitioners that there were too many risks attached to its use as a general narcotic for the dog.

The lack of literature on its use as an efficient anæsthetic led the present writers to carry out this investigation in order to show if chloral hydrate could be used as an intravenous general anæsthetic in dog practice in Egypt.

Material and Method

(*a*). *Preparation of the Animal.*

(1). The experimental dogs were in normal condition of health.

(2). They were kept fasting 24 hours before injection.

(3). Each dog was weighed in kilograms.

(4). The hair over the vein (either the saphenous or the cephalic) was clipped and the site cleansed with alcohol.

(5). A syringe with an eccentrically-placed nozzle for intravenous injection and needles sterilised by boiling were used.

(6). The dose of chloral hydrate was assessed according to the weight of the animal and injected slowly intravenously. The time allowed was approximately one minute.

(*b*). *Preparation of the Solution.*

(1). The drug and other ingredients were weighed and dissolved in distilled water which was sterilised by boiling.

(2). The solution was restored to its original volume and was allowed to cool to body temperature.

(3). The concentration of chloral hydrate used was 30 per cent solution freshly prepared (chloral hydrate 30 gm., sodium citrate 3 gm., sodium chloride 3 gm., distilled water 100 c.c.).

Experimental

(1). *Determination of the Anæsthetic Dose.*

Preliminary experiments showed that when chloral hydrate was used in the dose of 0.2 gm. per kilo body weight and its concentration in the solution was 20 per cent, it failed to produce anæsthesia of long duration in dogs (from 10 to 20 minutes). On doubling the dose of chloral hydrate, while the concentration remained constant, 70 per cent of the animals died. This indicates

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that 0.4 gm. chloral hydrate per Kilo B/Wt is too high. The authors then decided to increase the concentration of the solution to 30 per cent and lessen the amount of chloral hydrate given per kilo B/Wt. Animals were divided into groups of ten to find out the approximate anæsthetic dose.

Group I. Each individual received 0.3 gm. of chloral hydrate per kilo B/Wt. It was found that all animals survived the dose and were anæsthetised for a long duration ranging between 60-85 minutes.

Group II. The dose of chloral hydrate given to this group was raised to 0.31 gm. per kilo B/Wt. The animals were anæsthetised, and one death was recorded.

Group III. Increasing the dose of chloral hydrate to 0.32 gm. per kilo B/Wt, caused some losses raising the percentage of deaths. The authors estimated that the approximate anæsthetic dose is 0.3 gm. per kilo B/Wt.

Group IV. On decreasing the dose given to this group to 0.29 gm. chloral hydrate per kilo B/Wt, it was noticed that the duration of anæsthesia became somewhat shorter, ranging between 40-60 minutes.

From these experiments, the authors noticed that doses of chloral hydrate per kilo B/Wt under 0.3 gm. were not sufficient to produce maximum anæsthesia, and also that when the dose was increased to over 0.3 gm. it became toxic. A confirmatory experiment was performed on a group of 30 dogs of various ages and sexes.

The following conclusions were drawn from the previous results and observations:—

(1). The anæsthetic dose was estimated to be 0.3 gm. per kilo B/Wt.

(2). The duration of anæsthesia ranges between 60 to 85 minutes.

(3). After recovering from anæsthesia, the animal regained its consciousness, and became normal in a matter of minutes.

(4). The effect of the anæsthetic dose on respiration, pulse and temperature was very striking.

(*a*). The respiratory rate was diminished.

(*b*). The pulse became weak.

(*c*). The temperature fell.

(5). The muscles were completely relaxed and the pupils contracted during anæsthesia.

(6). All reflexes were absent. The pedal reflex was the last to disappear.

(7). In some animals, salivation, defæcation, micturition and vomition were observed.

II. Determination of the M.L.D.

As the anæsthetic dose of chloral hydrate in dogs was estimated, an attempt was made to determine the minimum lethal dose.

Experimental

The experimental dogs were divided into several groups beginning with that receiving 0.45 gm. of chloral hydrate per kilo body weight and ending with that receiving 0.33 gm.

All dogs injected with doses of 0.45 gm to 0.40 gm. per kilo B/Wt died, either during injection or immediately after; this showed that the M.L.D. was decidedly below these doses.

The survival of two out of five dogs injected with 0.39 gm. per kilo B/Wt denoted that this dose might be regarded provisionally as the M.L.D. To ascertain more accurately the M.L.D., 16 dogs were used and each individual was injected with 0.39 gm. per kilo B/Wt. This experiment resulted in the death of half of the animals injected and deep anæsthesia of long duration in the other half. Survival of 50 per cent of the dogs injected with 0.39 gm. per kilo B/Wt, indicates that this dose is the M.L.D. of chloral hydrate for dogs when given intravenously.

The doses 0.38 to 0.33 gm. of chloral hydrate per kilo B/Wt injected in members of the other groups, produced anæsthesia which varied in duration and depth according to the dose. There were some deaths; the losses varied according to the amount of chloral hydrate given.

Discussion and Summary

Although the dose of chloral hydrate assessed by Kaufmann depends on the size of the animal, yet from a practical point of view it cannot be relied upon as it was not determined according to the body weight of the animal. In Hoare's Veterinary Materia Medica and Therapeutics (1942) there is neither mention of chloral hydrate as an anæsthetic for dogs nor of its use when injected intravenously. It is stated in that book that the dose of chloral hydrate administered orally ranges from gr. v-xx. It is used combined with bromides for the control of the spastic convulsions in puerperal eclampsia in the bitch. In Hobday's Surgical Diseases of the dog and cat (1947), it is stated that the intravenous method of administration in a small animal like a dog or cat has too many risks attached to it to become popular with the general practitioner.

In the human subject, as stated in Cushny's Pharmacology and Therapeutics (1941), the use of chloral hydrate as an anæsthetic would be quite unjustifiable, because it is impossible to adjust the dose accurately enough to allow of complete anæsthesia without danger of respiratory failure.

The present work shows the possibility of the use of chloral hydrate as an effective anæsthetic in dogs when injected intravenously. The dose was estimated according to the body weight and was found to be 0.30 gm. per kilo body weight. When injected slowly and carefully, the authors did not notice any ill effect, however if some of the solution escaped subcutaneously the danger of sloughing is ever present. The above-mentioned anæsthetic dose of chloral hydrate could be applied in dogs from 6 months upwards. Major operations were performed after the administration of this drug such as laparotomy (ovariotomy and ovarohysterectomy of the pregnant uterus) in bitches, and castration in dogs. On two occasions hysterotomy was performed and the puppies were removed alive and destroyed after 24 hours.

Chloral hydrate could be used in Cæsarian section where it is desired to save the puppies. The margin of safety between the M.L.D. of chloral hydrate

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in dogs and the anæsthetic dose is somewhat wide and thus adds to the safety factor.

Acknowledgments

Our thanks are due to Professor El Said Fouad, Dean of the Faculty of Veterinary Medicine for his help and encouragement.

REFERENCES

Cushny, Arthur R. (1941): "Cushny's Pharmacology and Therapeutics." 12th edn., p. 328. London: J. A. Churchill, Ltd.

Greig, J. Russell and Boddie, George F. (1942): "Hoare's Veterinary Materia Medica and Therapeutics," 6th edn., p. 197-199. London: Baillière, Tindall & Cox, Ltd.

McCunn, James (1947): "Hobday's Surgical Diseases of the Dog and Cat," 5th edn., p. 47. London: Baillière, Tindall & Cox, Ltd.

REVIEWS

The Slaughter of Horses

BRITISH people make much of their animals and abhor cruelty in any shape or form.

Any evidence of cruelty to an animal elicits an immediate response and stout effort is made to bring relief to the sufferer and requisite punishment to those responsible.

There are times when this reaction amounts to hysteria and it is indeed fortunate that the final judgment rests with the Law which is propounded in the calm arena of Parliament.

The horse and the dog hold pride of place above all other animals in the public esteem and sentiment and there is no doubt that this extreme depth of feeling is tinged and actuated by the fact that we attribute to these animals reactions and feelings similar to those experienced by man.

During the last decade, owing to the advance of mechanised forms of transport and traction and also because of the shortage of protein of animal origin, we have witnessed the greatest destruction of equine life that has ever occurred in these islands. Beginning in or about the year 1940 the slaughter has been prodigious and it rose to its peak in 1948 when approximately 76,000 horses were slaughtered for food. Almost as many were disposed of in knacker yards.

It is natural that people of a horse-loving race should show due reaction in spite of the fact that the two factors which led to this carnage, redundancy, and shortage of meat, were coincident. The slaughter was widespread throughout the land and gathering impetus it reached the status of a holocaust. Horsemen and horse lovers were distressed and it was not long before rumours of acts of cruelty began to be spread abroad and the hearts of sensitive men and women were sorely troubled, and action to abate this evil was demanded in Parliament. As a result official investigations have been conducted on two occasions, in 1950 by a Departmental Committee on the Export and Slaughter of Horses and in

1953 by the Committee of Inquiry into the Slaughter of Horses. The Earl of Rosebery acted as chairman in 1950 and the Duke of Northumberland in 1953 and it is convenient to refer to the reports as those of the Rosebery and Northumberland Committees.

The two surveys covered a very wide field. On one vital point the two committees agree in that there was no evidence of cruelty at the time of the actual killing of the horses. The Northumberland committee found no evidence of the use of an electric pump for the extraction of blood nor of illegal methods of slaughter.

In the view of this committee " The risk of cruelty is not so much in the actual method and act of slaughter but in connection with the transport, handling, lairaging, feeding and watering of horses destined for and awaiting slaughter and is more often than not due to carelessness or omission to take steps for the animal's " comfort."

They report that " There is undoubtedly considerable room for improvement in these directions and we make proposals to this end."

There can be no doubt that these words go to the very crux of the matter, and their recommendations will meet with the full support of all humane people.

Horses and dogs have lived so long in such close association and contact with man that we are apt to attribute to them almost the same measure of intelligence, sentiment, apprehension and sensory reaction as is developed in humans. There is no doubt that if a man were escorted to a house of human sacrifice or slaughter he would experience great mental torture and especially so if he had to thread his way through the mortal remains of previous victims. Does a horse experience this mental torture, can he recognise the remains of his fellows, does he know that he is doomed?

Scientists may say " No," sensitive humanitarians say " Yes," just as positively. The truth is that this is one of the questions which, in the state of present knowledge cannot be answered one way or the other with any degree of certainty. The sensible attitude in all cases of doubt is to give the benefit to the victim or the accused. In this case the horse, our friend, is the potential victim and we should take every precaution to see that when the time comes for him to pass on there shall be nothing to disturb his physical or mental peace. If at some later date our scientists can prove conclusively that all these precautions were unnecessary then we have lost nothing, if their researches should prove the reverse and we have neglected to help our friend in his distress then in our memories and conscience we will quite rightly suffer the torture of the damned.

The slaughter of the majority of our horses is inevitable. They are the victims of the triumphal progress of the internal combustion engine, an instrument which has brought great good and great harm to the world. The horses figure on the debit side and it is our duty to see that our friends can lay down their burden in peace.

The Report of the Northumberland Committee of Inquiry into the Slaughter of Horses was presented to Parliament by the Minister of Food and the Secretary of State for Scotland by Command of Her Majesty. August, 1953. Copies can be obtained from Her Majesty's Stationery Office, London. Price 1s. 9d. net.

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McFadyean's Osteology and Arthrology of the Domesticated Animal, by H. V. Hughes and J. W. Dransfield. 4th Edition. London: Baillière, Tindall & Cox Ltd. Price 21s. net.

A sound knowledge of the skeleton is the basis of Anatomy.

This statement applies with particular emphasis to the study of Veterinary Anatomy. Veterinary students should remember that lesions and abnormalities of the locomotor system will claim much of their attention when they practice as Veterinary Surgeons.

McFadyean's "Osteology and Arthrology" has been recognised as a "classic" for many years. The last edition was a reprint, and dated 1934. For many years it has not been possible to purchase a new book, and second-hand copies have been in very short supply. No other book just fills the niche which this one has occupied for so long and so teachers and students will welcome this new edition of an old friend.

Though the size remains as of yore the text has been completely revised. Terminology has been modified to suit present-day systems, and more attention has been paid to the development of bones.

The illustrations have been re-drawn, for the original "stones" from which they were printed were no longer serviceable. Many new figures have been added. It is a pity that these excellent illustrations had to be reduced so much in size; it is almost necessary to use a magnifying glass to appreciate some of the detail.

We have waited a long time for a new edition of this useful book. The Editors have done a good job and have earned the thanks of students and teachers. The Publishers must be thanked for taking on the task of providing us with a new edition of an essential textbook, and they can be congratulated on the way in which they have done the work.

We hope that a new edition of McFadyean's other classic, "The Dissection of the Horse," will also occupy their generous attention.

The Artificial Insemination of Farm Animals. Edited by Enos J. Perry. Second Revised Edition—1952, Illustrated, 341 pages. New Brunswick: Rutgers University Press. Price $5.00.

This is the second edition of a book first published in 1945 and previously reviewed in *The Veterinary Journal, 102,* p. 182. The subject matter of all chapters has been revised and extended and brought abreast of the latest developments in artificial breeding techniques. The scope of the first edition has now been widened, thus greatly enhancing its value as a reference manual by the inclusion of new chapters on "The Role of Hormones in Reproduction," "Factors Influencing Quality and Quantity of Semen," and one dealing with artificial insemination in the dog.

In view of a minor criticism made in our notice of the first edition relating to the chapter on "Disease in Relation to Artificial Insemination," it is pleasing

to record that in the second edition this chapter has been written by a veterinary surgeon—and one, moreover, who is well-known in England for his work on artificial insemination. On the other hand, several errors of fact which were noted in the first edition have been repeated in the second.

The clarity of the text has been improved by the addition of several excellent new figures and diagrams.

We commend this second edition of "The Artificial Insemination of Farm Animals" to all interested in the art and science of animal breeding. In our opinion it is the best available exposition of the subject within the covers of one book, dealing with all the species of farm animal as well as including chapters on birds and dogs.

THE DISTEMPER COMPLEX, by Leon F. Whitney, D.V.M. and George D. Whitney, D.V.M. Orange, Connecticut. Practical Science Publishing Company. Pp. 219. Price 40s. net. Distributors in U.K.: Bailey Bros. & Swinfen Ltd., London.

THE authors are convinced that the term distemper encompasses many diseases other than the traditional "distemper" of old. Accordingly an account is given of eleven conditions in the dog ranging from the classical canine distemper to hard-pad and on through infectious hepatitis to toxoplasmosis and leptospiral infections. The bibliography contains about 1,500 references and each account takes cognisance of the history, symptoms, diagnosis, pathology and treatment of the eleven conditions. The style of writing is rather "racy" in places and an appeal is made to the informed layman but in spite of this there is so much value in the work that the small animal practitioner will find it useful and interesting. It is irritating to find that B.S.D. is used to mean "before sulfa drugs" and that B.A. means "before antibiotics" but these are minor criticisms allied to the spelling which is different from that to which we are accustomed.

THE WAY OF A HORSE, by Marguerite de Beaumont. London: Hurst & Blackett Ltd. Price 15s. net.

THE dust jacket attracted me, the interior intrigued me, and by reading it I gained much profit.

This book is different from most horse books, for it is not just a collection of repetitive "do's and don'ts." It is written in an easy philosophical conversational style, and one could well imagine that one was in a group sitting around the saddle room fire and listening to the author describing incidents, and passing on a fund of stable lore garnered and sifted by an acute observer who started from scratch and has earned recognition as a top class authority.

Every facet of equine husbandry and horsemastership is touched upon, and the reader's interest is held from start to finish. The illustrations have been selected with care. They are all good, but I found that I was continually turn-

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ing for another look at the one opposite page 157, that is "Honeysuckle, Hack of the Year 1952."

Young and old, the experienced and the novice, can read this book with pleasure and profit.

CANINE SURGERY, A TEXT AND REFERENCE BOOK, the work of 29 North American authors. Edited by T. V. Lacroix, D.V.S. and H. Preston Hoskins, V.M.D., Evanston, Illinois. American Veterinary Publications. Price $15.50. U.K. £5 17s. 6d. net.

THE third edition of this book is certainly a great improvement on previous issues. The general format follows that of most surgical textbooks and the various techniques are arranged in a systematic regional plan. The first chapter gives a general review of the salient gross anatomical features of the dog, and chapter two, headed "Physiology," gives interesting information on blood.

Chapters 3-9 deal with such matters as healing and repair, infective processes, sterilisation, general surgical technique and anæsthetic methods. Wound protection, the physiology of some post-operative conditions such as shock and blood transfusion, take the discussion along to the general consideration of traumatic injuries and the neoplasms.

Chapter 13 gives a very interesting and informative account of canine dental surgery.

The various chapters devoted to the surgery of specific regions and tissues make most interesting reading and as each section has been contributed by a surgeon who has devoted much of his energy to the part under discussion they contain a wealth of up-to-date information.

As there are many authors and no one can claim to be an expert in every branch of canine surgery it would be invidious to try and classify their writings in order of merit but certain chapters appeal to the reviewer, namely those on the ear, the eye and fractures.

I doubt if better expressions can be found. To sum up, the editors have attempted to produce a canine Rose and Carless and to do this they have sought the help of acknowledged specialists.

They have gone far towards success and the only real criticism I will make is this, that they have produced a specialist postgraduate book which is too full of intricate detail to be of great value to a student who has, in the short time at his disposal, to master the basic fundamental principles of general veterinary surgery.

THE ANATOMY OF THE DOMESTIC ANIMAL, by Septimus Sisson, S.B., V.S., D.V.Sc. Revised by James Daniel Grossman, G.Ph., D.V.M., Professor of Veterinary Anatomy, Ohio State University. W. B. Saunders & Co., London and Philadelphia. Price 75s. net.

SEPTIMUS Sisson's Anatomy of the Domestic Animal stands so high amongst the list of recognised classics in Veterinary literature that it has achieved the

status of a Bible in the English speaking Veterinary Schools throughout the world.

Since Sisson's death in 1924 the task of editing and supervising its contents has been in the hands of Prof. James D. Grossman and this, the fourth edition of the work, is a manifest tribute to the success which has attended his labours.

The terminology, always a troublesome matter to veterinary students, has been brought completelv into line with the systems which have now achieved general acceptance.

The illustrations were always superb and Dr. Grossman has been able to add many more of equal merit. These illustrations alone justify the purchase of the book, and enable a student to revise his knowledge of Veterinary Anatomy during those hours of concentrated effort when he burns the midnight oil and is far removed from the actual specimens. The frontispiece depicting Professor Sisson and giving an account of his life and work is a worthy token to a great man who did so much in his relatively short life to advance Veterinary Science.

THE SULPHONAMIDES AND ANTIBIOTICS IN MAN AND ANIMALS, by J. Stewart Lawrence, M.D.(Ed.), M.R.C.P., and John Francis, M.Sc., M.R.C.V.S., with the assistance of Arnold Sorsby, M.D., F.R.C.S. and Peter G. Scott, F.R.C.S. London: H. K. Lewis & Co. Second Edition 1953. Pp. xii + 482. Illust. 39 in text and plates. Price 42s.

THE tone of this book is set by the opening sentence in the preface to the second edition which reads: "When this book was first conceived some seven years ago, the sulphonamides were alone available for the effective treatment of bacterial infection, though the value of penicillin had already begun to emerge." It is difficult to know for whom the book is written; it contains masses of information about the sulphonamides, the sulphones, the thiosemicarbazones, para-aminosalicylic acid and isonicotinyl. The antibiotics considered are terramycin, aureomycin, chloromycetin (chloramphenicol), neomycin, streptomycin and penicillin. The first twelve chapters are given over to the drugs, their chemistry and pharmacology, their effect upon specified bacteria, their toxic effects and general indications for their use. Accounts are given, from chapter thirteen onwards, of the uses of the different drugs in streptococcal infections, in staphylococcal infections and in those conditions in man caused by other bacteria, the rickettsiae, viruses and spirochætes. A few of the later chapters deal briefly with diseases of the eye, nose or skin; two deal with veterinary medicine and one with laboratory tests. All this in a little under 500 pages.

We are told in the preface that "emphasis is chiefly on the clinical aspect and on the practical application of antibacterial agents to the control of natural infections"; furthermore, that the bacterial nomenclature used is that recommended by the American Society of Bacteriologists. There are forty-one pages of references to original work and yet the book is in some way a disappointment. There is a lack of criticism of the work cited and even when the authors purport

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to give a summary, or advise as to the routine treatment of a patient the reader is left with an uncertainty as to what it all means. In spite of the wording of the preface there is a lack of the appreciation that the physician has to treat patients and the " cure of the disease more grievous than the endurance of the same " becomes a fear (see *Brit. med. J.*, 1953, 671). It is also clear that the text needs editing and co-ordination. *B. mallei* is not the name used by the American Society of Bacteriologists; *" Erysipelothrix* and *rhusiopathiae "* is meaningless and *" Salmonella gaertneri "* is an obsolete term. On page 130 we read that *Erysipelothrix monocytogenes* is susceptible to a concentration of streptomycin which differs from that of *Listeria monocytogenes;* are not these the same bacterium? *Salmonella typhosa* and *Salmonella typhi* appear within a few pages of each other and *Salmonella paratyphi* and *Salmonella Schotmülleri* jostle each other. It is a little surprising to find that the dramatic effect of sulphaguanidine in the form of dysentery due to Shiga's bacillus is treated so cursorily; the influence it had in some of the theatres of war should have made it worthy of more attention.

The two chapters on the veterinary aspects do not give any greater satisfaction; didactic statements are made in the introduction of chapter 28 and the comparisons made between human and animal infections could be challenged. The impression appears here also, that the maximum amount of original work must be mentioned but it is not assessed and consequently the practitioner receives less help than the authors intended.

It is a little sweeping to say that " Pyelonephritis caused by *C. pyogenes* responds . . . " and in the section on anthrax to add: " Without treatment, it is unusual for animals to recover." Is it wise to refer to the *Anatipestifer* group of bacteria and then spell *Pfeifferella* wrongly when explaining it? The hurried preparation of the book is also patent when the bibliography is examined. The reference in the text to an analysis by Raistrick cannot be found in the bibliography and it means the work reported by Clutterbuck, Lovell and Raistrick—all readers would not know this. The name of Andrewes is spelt wrongly in the text, though correctly in the bibliography. The initials and the spelling of the name Cruickshank need correction—there are two errors in the bibliography concerning those authors with this name and the reference to La Bocetta and Lockwood 1944 could not be found. It is very regrettable that the vast amount of reading and the industry of the authors has not yielded something more valuable and advantageous to those who want to know more about modern therapy.

NEWS

NEW APPOINTMENTS

Dr. D. W. Adamson, M.Sc., D.Phil., A.R.C.I., formerly head of the Chemical Division of the Wellcome Research Laboratories, Beckenham, has been appointed Research Director of the Wellcome Foundation Ltd. and

Director of the Wellcome Research Laboratories as from September 1. Dr. Adamson has also been appointed to the Board of the Wellcome Foundation Ltd.

Miss O. Uvarov, M.R.C.V.S., recently joined the technical staff of the Veterinary Department of Glaxo Laboratories Ltd. as assistant to Mr. Neil Mathieson, M.R.C.V.S.

RETIREMENT

Dr. J. W. Trevan, M.B., B.S., B.Sc., F.R.C.P., F.R.S., Research Director of the Wellcome Foundation Ltd., and Director of the Wellcome Research Laboratories, Beckenham, and a member of the Board retired from these appointments on August 31, after more than 33 years' service with the company.

NEW PRODUCTS

Genatosan Ltd. announce the introduction of a new and greatly improved Blackleg Vaccine which is being marketed as Blackleg Vaccine A.P.A. Genatosan.

Supplied in bottles of 50 c.c. it is claimed that this Vaccine produces a high degree of immunity 10-14 days after inoculation. The Vaccine is safe to use and there is no local or systemic reaction. List price 7s. 3d. per 50 c.c.

Glaxo Laboratories Ltd., Greenford, Middlesex, announce the introduction of Veterinary Mylipen, an aqueous suspension of procaine penicillin G. This new veterinary pack will be available as a multidose 30 c.c. rubber capped bottle (Silicone treated). Each c.c. contains 300,000 units procaine penicillin G.

Burroughs Wellcome & Co. announce that " Epivax " Canine Distemper Vaccine, Egg-Adapted (Living) is now available to members of the Veterinary profession for the prevention of distemper and hard pad disease. This is a special strain of virus which is propagated in fertile eggs and which by serial passage has lost its virulence, but retained its antigenicity. It thus dispenses with the need for vaccine or serum in prophylaxis. Only one injection is necessary, but in puppies younger than 12 weeks, a second dose is recommended about 2 months after the first. " Epivax " is non-infective to susceptible puppies and the injected dog is not a source of risk to contacts. " Epivax " is also recommended as a therapeutic agent in the treatment of distemper and hard pad disease.

" Epivax " is prepared at the Wellcome Research Laboratories and is available as freeze-dried material in unit packs of one ampoule, with an ampoule of diluting fluid.

The life at cool-room temperature is one month, but in the freezing area of a domestic refrigerator " Epivax " will retain full potency for at least three months.

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BURROUGHS Wellcome & Co. announce the installation of a teleprinter at their head office, 183-193 Euston Road, London, N.W.1, to expedite the arrival of inland telegrams. The telegraphic address is now Tabloid London Telex.

A NEW film entitled "Nalorphine" ("Lethidrone") has been produced by the Wellcome Film Unit in collaboration with The Wellcome Research Laboratories. This describes the action of nalorphine (N-Allylnormorphine) in antagonising the effects of morphine and other drugs with a similar action. The film is in colour, with sound, and runs for 10 minutes.

The film demonstrates the dramatic recovery which results when intravenous nalorphine is given to dogs deeply narcotised with morphine, methadone ("Physeptone") and thiambutene ("Themalon"), a new analgesic recently introduced into veterinary practice.

The groups of drugs which act in the same way as morphine are listed for it is only these which are specifically antagonised by nalorphine.

The film may be borrowed on application to the Public Relations Officer, Burroughs Wellcome & Co., 183-193 Euston Road, N.W.1.

PRICE REDUCTIONS

AMONG penicillin products reduced in price from August 31 is the 8-oz. container of Veterinary Penicillin Granules Glaxo. This preparation, containing 2.5 per cent w/w procaine penicillin, is primarily intended for the prophylaxis and treatment of calf and pig scours and other intestinal infections, and is specially prepared to mix easily into the food or drink.

THE Distillers Company (Biochemicals) Ltd., Speke, Liverpool 19, on behalf of its distributors: Allen & Hanburys Ltd., The British Drug Houses Ltd., Burroughs Wellcome & Co., Evans Medical Supplies Ltd., Imperial Chemical (Pharmaceuticals) Ltd., and Pharmaceutical Specialities (May & Baker) Ltd., announces reduced retail prices of the following penicillin products:—Penicillin G, Sodium salt and Potassium salt (buffered) 'Distaquaine' G, 'Distaquaine' Suspension, 'Distaquaine' Fortified, Streptomycin (sulphate) and Dihydrostreptomycin (sulphate), 'Distavone,' 'Mixtamycin,' 'Streptaquaine.'

Publishers' Notices

THE BRITISH VETERINARY JOURNAL, with which is incorporated THE VETERINARY JOURNAL, is published monthly, and copy for advertisements should be in the hands of the advertisement manager not later than the 20th of the preceding month, if proof is required. Tel.: Temple Bar 3386.

Letters for the Journal, literary contributions, reports, notices, books for review, exchanges, new instruments or materials, and all matter for publication (except advertisements) should be addressed to the Editor.

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